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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,734	08/15/2001	Raymond F Horvath	98,313-C	3870

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	PAPER NUMBER
1624	4

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/930,734	HORVATH, RAYMOND F	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,12-19,22-27,29-50 and 52-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 12-19, 22-27, 29-50, and 52-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a continuation of application 09/561,569 (now US Patent No. 6,284,766). With claims 10, 11, 20, 21, 28, and 51 cancelled, only claims 1-9, 12-19, 22-27, 29-50, and 52-67 remain for consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 3, 6, 7, 18, 19, 23-27, 29, 30-34, 38, 39, 43, and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

   a. Claims 3, 6, 7, 18, 19, 23-27, 29, 30, 32, 33, 34, and 43 recite the limitation "R^8 is hydrogen" in their tricyclic compounds. There is insufficient antecedent basis for this limitation in said claims because hydrogen is not in the definition of R^8 as recited in claim 1. Note, claims 18, 19, 23-27, 29, 30, 32, 33, 34, and 43 do not recite the limitation, "R^8 is hydrogen"; however, they recite species of "...-9H-pyrimidino[4,5-b]indole" which suggests R^8 as hydrogen.

   b. Claims 31, 38, and 39 recite the species of "...-5,6,7-trihydrocyclopenta[2,1-d]pyrimidino[4,5-b]indole" which suggests a tetracyclic system. There is insufficient

antecedent basis for this limitation in said claims because, as recited in claim 1, R^2 and R^3 do not form a bicyclic system.

c. Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. See MPEP § 2172.01. The omitted steps are those related to ring fusion, amination, alkylation, etc.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following factors have been considered in the determination of an enabling disclosure:

(1) The quantity of experimentation necessary;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The breadth of the claims;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

2. **Enablement:** Claims 31, 38, and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. No preparation and use are provided for compounds of a tetracyclic system (i.e., '5,6,7-trihydrocyclopenta[2,1-d]-8H-pyrimidino[4,5-b]indole'). Although the preparation of said species is referred to Example 1, one skilled in the art cannot obtain this complicated tetracyclic system without undue experimentation. Note, the starting material in Example 1 is a substituted '4,5,6,7-tetrahydro-indole', which ultimately gets cyclized to become 'pyrimidino[4,5-b]indole' – a tricyclic system, not a tetracyclic system. There is no suggestion on how one can obtain the starting material for a tetracyclic system, or if such a starting material is commercially available. Thus, with the unpredictable nature of the art, undue experimentation is inevitable for one skilled in the art to make and use said tetracyclic species. See, **In re Howarth, 210 USPQ 689; In re Lund, 153 USPQ 625; In re Fouche, 169 USPQ 429,** regarding how to make and use.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 2, 8, 9, 53, 64, and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 8-11 of U.S. Patent No. 6,284,766. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter claimed herein embraces the one in US'766.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-7, 12-15, 17, 18, 22, 24, 27, and 53-67 are rejected under 35 U.S.C. 102(a) as being anticipated by **Tanaka et. al.** (WO 98/29397 or WO'397 – cited on IDS). On pages 40 and 41, Tanaka et. al. disclose two formulae (43) and (44) that are embraced by the scope of the formula recited in claims 1-7, and 12-14 – particularly, when the claimed formula has the following substitutents:

i. Ar represents a phenyl group;

ii. R^2 and R^3 form a cyclohexyl or benzo;

iii. R^1 is an alkyl group.

Furthermore, species in claims 15, 17, 18, 22, 24, and 27 are disclosed as compounds 46, 42, 47, 44, 51, and 45 (respectively) in WO'397 (see pages 41, 113, 115-117, and 119). Claim 53 is a pharmaceutical composition which is apparently disclosed on page 46 because a dosage of 0.01 – 300 mg/person/day is stated on lines 7and 8. Claim 54 recites a process of making the claimed formula which is described on pages 39-41. Claims 55 and 56 are inherently embraced as it is well known that a package of a pharmaceutical product requires a container and an instruction. Claim 57 is a method of assaying the affinity of the claimed compounds for CRF receptor, and said method appears on page 121 of WO'397. Claims 58-60, and 64-67 are drawn to methods of inhibiting CRF receptors (or altering signal transducing activity on said receptors), and treating related disorders. Said methods of use can be found throughout the document (see English abstract). Finally, compounds in claims 61-63 are embraced by the disclosed compounds as they have an IC_{50} of less than 500 nM (see page 122, lines 1 and 2). Thus, at the time of the invention, one skilled in the art would have known how to make and use tricyclic compounds as claimed herein in view of Tanaka et. al.

5. Claims 1-4, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by **Müller et. al.** (J. Med. Chem., 1990, Vol. 33 (10), pp. 2822 – 2828). In Table 1, Müller et. al. disclose compound #5 (type II, and type III), which is embraced by the claimed formula with the following substituents:

iv. R^1, R^4, and R^5 represent hydrogen;

v. Ar represents a phenyl group di-substituted with C_1-C_6 alkoxy.

Thus, at the time of the invention, one skilled in the art would have known how to make a tricyclic compound with such substituents in view of Müller et. al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-7, 12-14, 16, 19, 22-27, 29, 30, 32-37, 40, 43-50, and 52-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Tanaka et. al.** Besides the species discussed in the 102(a) supra, Tanaka et. al. also provide two generic formulae (i.e., compounds #43, and 44) which allow for various permutations as their variables represent more than one moiety. The scope of said formulae overlaps with that of the claimed formula recited in claims 1-7, 12-14, and embraces species in claims 16, 19, 22-27, 30, 32-37, 40, 43-50, and 52. Composition and method claims are taught by Tanaka et. al. as mentioned in the 102(a) supra. Thus, at the time of the invention, it would have been obvious to one of ordinary skill in the art to make and use tricyclic compounds other than those anticipated by Tanaka et. al. (e.g., those with R^1 as

hydrogen). Note, the generic teaching of Tanaka et. al. would have allowed one skilled in the art to select compounds of the above claims, and expect them to inhibit CRF receptors as well. Moreover, such an issue of patentability has also been decided by the court in In re Susi, 440 F 2d. 442, 445, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in Merck & Co. v. Biocraft Laboratories, 874 F 2d. 804, 10 USPQ 2d. 1843, 1846 (Fed. Cir. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Tamthom N. Truong
Examiner
Art Unit 1624

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February 21, 2003